

We claim:

1. A sustained release formulation with dimethicone as dispersing agent, comprising:

- a. a therapeutic drug or active ingredient 0.5-40%, W/V;
- b. dimethicone to the final volume; and

5 c. optionally, a suitable adjuvant such as stabilizer, antioxidant, local analgesics or material for sustained release.

2. The formulation of claim 1 wherein said therapeutic drug or active ingredient is selected from the group comprising:

- 10 (1) Avermectins including abamectin, ivermectin, emamectin, eprinomectin, doramectin, moxidectin, and 4''-O- carbamylmethyl- avermectin B₁, and other avermectin derivatives;
- (2) Nonsteroidal anti-inflammatory including salicylates, pyrazolones, p-aminophenol derivatives, indole, indan acetic acid, aryl alkanoic acids (e.g. mixed aryl acetic acids, and arylpropionic acid), 1,2-benzothiazin, fenamic acids (e.g. enol acids, alkyl ketone), anthranilic
- 15 acids (belonging to fenamic acids) and other COX-2 inhibitors, preferably, indomethacin, ketoprofen, flunixin, diclofenac and piroxican;
- (3) Other parasitocides including imidacloprid, diflubenzuron, lufenuron, methoprene, fipronil, pyriproxyfen, cyromazine, toltrazuril, diclazuril, closantel, closantel sodium, albendazole, and albendazole sulfoxide hydrochloride, which be combined with avermectins to make a
- 20 compounded injection formulation.
- (4) Antibiotics, including cephalosporins, penicillins, β -lactamase inhibitors, thiamuline, tiamulin fumarate, tylosins (e.g. tilmicosin, acetyl isovaleryl tylosin), doxycycline, doxycycline hydrochloride, minocycline, gentamycin, lincomycin, clindamycin, neomycin, polymyxin, quinolones, sulfanilamide, which can be used alone or in combination in the formulation;
- 25 (5) Sex hormones including estrogen, progesterone and androgen;
- (6) Oil soluble vitamins; and
- (7) Mineral elements insoluble in water or slightly soluble in water.

3. The formulation of claim 1 wherein said stabilizer and material for sustained release is non-ionic surfactant, suspension –assisting agent, hydrophilic material for sustained release or hydrophobic material for sustained release.

4. The formulation of claim 3, said non-ionic surfactant, suspension –assisting agent, hydrophilic material for sustained release or hydrophobic material for sustained release is selected from the group consisting of: glycerol fatty acid esters, polyglycerol fatty acid esters, sugar ester, sorbitan fatty acid esters(Span), polyoxyethylene sorbitan fatty acid esters (Tween), Myrjs, Brijis, Paregal, OP, polyvinyl chloride castor oil, condensation compound, polyvinyl chloride hydrogenated castor oil, condensation compound, Pluronic, fatty acid esters which exists in the form of solid at the temperature below 40°C (e.g. glycerol monostearate, hydrogenated castor oil and carnauba wax ect.), lanolin, stearic acid, cetyl alcohol, poly vinyl pyrrolidone (PVP), polyethylene glycol (PEG) with MW larger than 1000, gelatin, gum Arabic, ethylcellulose, polyvinyl butyral. Particularly preferred stabilizer and material for sustained release thereof comprises Tween, Span, ethylcellulose, hydrogenated castor oil, aluminium stearic acid, PVP and PEG (MW larger than 1000), which can be used alone or in combination.

5. The formulation of claims 1-4, characterized in that the formulation comprises:

- a. avermectins 0.5-30%, W/V;
- b. hydrogenated castor oil 0-10%, W/V;
- c. local analgesics 0.5-2.5% W/V;
- d. BHT, BHA, PG, or the combination 0.2%, W/V; and
- e. dimethicone to the final volume.

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6. The formulation of claim 5, comprising:

- a. avermectins 1-10%, W/V;
- b. hydrogenated castor oil 1-5%, W/V;
- c. trichlorobutanol 0.5%, W/V;
- d. BHT/BHA/PG 0.2%, W/V ;
- e. dimethicone with viscosity less than 100mm²/S to the final volume.

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7. The formulation of claim 6, characterized in that the formulation is prepared by the following methods:

Method (1): to a certain amount of avermectins adding alcohol (2-5 times the amount of

avermectins), acetone or another organic solvent with a low boiling point, with or without adding hydrogenated castor oil added; dissolving/melting the drug at the temperature of 85°C; let it cooling while stirring; then adding dimethicone to the final volume; removing alcohol, acetone or other organic solvent by lowering the pressure; and thereafter homogenizing (e.g.
5 by colloid mill or ball mill) to obtain a sustained release formulation.

Method (2): a certain amount of avermectins, adding a small amount of dimethicone and hydrogenated castor oil; melting hydrogenated castor oil at the temperature of 90°C; cooling with stirring to produce a paste-like viscous liquid; grinding (with a colloid mill or a ball mill) to the particle size of 100 micrometers, and then adding more dimethicone to the final
10 volume.

Method (3): Dispersing the micro powder of avermectins (particle size smaller than 100 micrometers) to melted hydrogenated castor oil; adding dimethicone; homogenizing; and thereafter adding more dimethicone to the final volume.

Method (4): Dispersing the solid dispersion comprising avermectins and hydrogenated
15 castor oil in dimethicone; heating with stirring at a temperature around 90°C; When the mixture is melted, let it cooling and continue stirring until the mixture is homogenized; and thereafter adding more dimethicone to the final volume.

Method (5): Dispersing the solid dispersion comprising avermectins and hydrogenated castor oil in dimethicone; grinding (with colloid mill or ball mill); homogenizing; and upon the
20 particle size reaching smaller than 120 micrometers, adding more dimethicone to the final volume.

8. The formulation of claims 1-4, characterized in that the formulation and method of preparation is as follows:

(1) formulation, comprising:

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| a. | Avermectins-carrier powder | 2-35% (W/V); |
| b. | Suspending agents (e.g. hydrogenated castor oil) | 0-3% (W/V); |
| c. | local analgesics | 0.5-2.5% (W/V); and |
| 25 | d. | dimethicone to the final volume; |

(2) method preparation, comprising the steps as follows:

Disperse avermectins-carrier powder (particle size less than 360 micrometer) in dimethicone;

grind until the particle size becoming smaller than 150 micrometers; then add and mix with dimethicone (with or without suspending agent therein) to the final volume. Or, Disperse avermectins-carrier powder (particle size less than 120 micrometer) in a sufficient amount of dimethicone with or without suspending agent therein; and then homogenize to obtain the
5 final product.

9. The formulation of claim 8, wherein said Avermectins-carrier powder is a solid dispersion comprising avermectins and carrier material for sustained release or another kind of carrier powder (e.g. microball, microcapsule or nanoparticle).

10. The formulation of claim 9, wherein said carrier material for sustained release can be hydrophilic or hydrophobic. Preferred hydrophilic material may be gelatin, gum Arabic, PEG (MW larger than 1000) or PVP. Preferred hydrophobic material may be ethylcellulose, polyvinylbutyral, or hydrogenated vegetable oil (e.g. hydrogenated castor oil). More preferred
15 hydrophobic material is ethylcellulose, hydrogenated castor oil, PEG (MW larger than 1000), and PVP, which can be used alone or in combination.

11. The formulation of claims 6-8, characterized in that it is suitable for the prevention and treatment of problems caused by parasites in animals, preferably by subcutaneous injection
20 and preferably at the site of the skin behind the ear, or on the neck or back, with possible dose range being 0.2-6 mg/kg (active ingredient / body weight), preferably 1-3 mg/kg.

12. The formulation of claims 1-4, characterized in that the formulation is as follows:

(a) NSAIDs 1-15%(W/V),

25 (b) hydrogenated castor oil 0-5%(W/V),

(c) dimethicone to the final volume, and optionally

(d) suitable adjuvant such as antioxidants and local analgesics.

13. The formulation of claim 12, characterized in that the preparation methods are as follows:

30 Method (1): to a suitable amount of NSAIDs, adding 2-5 times amount of alcohol, acetone or other organic solvent with a low boiling point; adding optional hydrogenated castor oil;

dissolving/melting the mixture at around 85°C; cooling by stirring; adding dimethicone to the final volume; removing alcohol, acetone or other organic solvent by reducing the pressure; and thereafter homogenizing (e.g. by a colloid mill) to obtain the final product;

Method (2): to a certain amount of NSAIDs and hydrogenated castor oil, adding a small

- 5 amount of dimethicone; melting hydrogenated castor oil at around 90°C; cooling by stirring to produce a paste-like viscous liquid; grinding (with a colloid mill or a ball mill) until the particle size becoming smaller than 100 micrometers; adding more dimethicone and adjuvant to the final volume;

Method (3): Dispersing a certain amount of micro powder of NSAIDs (particle size smaller

- 10 than 100micrometers) to melted hydrogenated castor oil; adding dimethicone; homogenizing; and thereafter adding more medium to the final volume;

Method (4): Dispersing a certain amount of NSAIDs /hydrogenated castor oil solid dispersion in dimethicone; heating with stirring at the temperature of 90°C or so; upon melting of the mixture, cooling it with stirring until it is homogenized; and then adding more medium and

- 15 adjuvant to the final volume; and

Method (5): Dispersing a certain amount of NSAIDs /hydrogenated castor oil solid dispersion in dimethicone; grinding (with a colloid mill or a ball mill); homogenizing; upon the particle size reaching 120 micrometers, adding more medium and adjuvant to the final volume.

- 20 14. The formulation of claims 1-4, characterized in that the formulation and methods of preparation are as follows:

Formulation, comprising:

(a) fipronil, diflubenzuron or imidacloprid 2-10%(W/V),

(b) hydrogenated castor oil 0.2-5%(W/V),

- 25 (c) dimethicone to the final volume, and optionally,

(d) suitable adjuvant such as antioxidant and local analgesics; and

Methods of preparation are as follows:

Method (a): to fipronil, diflubenzuron or imidacloprid, adding alcohol, acetone or another organic solvent with a low boiling point; adding hydrogenated castor oil; dissolving/melting the mixture at around 85°C; cooling with stirring; adding dimethicone to the final volume; removing

- 30 alcohol, acetone or other organic solvent by reducing pressure; and thereafter homogenizing

(e.g. by a colloid mill) to obtain the final products;

Method (b): adding a small amount of dimethicone to fipronil, diflubenzuron or imidacloprid and hydrogenated castor oil; melting hydrogenated castor oil at around 90°C; cooling with stirring to produce a paste-like viscous liquid; grinding (with a colloid mill or a ball mill) until
5 particle size becoming below 100 micrometers; and then adding more medium and adjuvant to the final volume;

Method (c): dispersing a certain amount of micro powder of fipronil, diflubenzuron or imidacloprid (fineness less than 100 micrometers) in melted hydrogenated castor oil; adding dimethicone; homogenizing; and then adding more medium to the final volume;

10 Method (d): dispersing in dimethicone a certain amount of solid dispersion of fipronil, diflubenzuron or imidacloprid and hydrogenated castor oil; heating with stirring at the temperature around 90°C; upon melting of the mixture, cooling it with stirring until it is homogenized; and then adding more medium and adjuvant to the final volume;

Method (e): dispersing in dimethicone a certain amount of solid dispersion comprising fipronil,
15 diflubenzuron or imidacloprid and hydrogenated castor oil; grinding (with a colloid mill or a ball mill); homogenizing; and when the particle size reduces to smaller than 120 micrometers, adding more medium and adjuvant to the final volume.

15. The formulation of claim 14, characterized in that the formulation and method of
20 preparation are as follows:

Formulation is follows:

(a) penicillin or cephalosporins 2-40%(W/V),

(b) hydrogenated castor oil 0-5%(W/V),

(c) dimethicone to the final volume, and optionally

25 (d) suitable adjuvant such as antioxidant and local analgesics.

Preparation Methods are as follows:

Method (a): adding a small amount of dimethicone to penicillin or cephalosporins to make a paste-like viscous liquid; optionally grinding (with a colloid mill or a ball mill); adding dimethicone that contains melted hydrogenated castor oil; dissolving/melting the mixture at
30 the temperature around 85°C; cooling it with stirring to make a viscous liquid; grinding (e.g. with a colloid mill or a ball mill) until the particle size reaches 100 micrometers; and adding

more medium and adjuvant to the final volume;

Method (b): dispersing a certain amount of micro powder of penicillin or cephalosporins (particle size smaller than 100 micrometers) to melted hydrogenated castor oil; adding dimethicone; homogenizing; and then adding the more medium and adjuvant to the final

5 volume; and

Method (c): adding a small amount of dimethicone to penicillin or cephalosporins to make a viscous liquid; grinding (with a colloid mill or a ball mill) until the particle size reaches 100 micrometers; and then adding more dimethicone and adjuvant to the final volume.